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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,102	05/01/2001	Dennis A. Carson	220002062900	5759
7590 10/18/2004 Kevin L. Bastian, Esq. Townsend and Townsend Crew LLP			EXAMINER	
			YU, MISOOK	
Two Embarcadero Center, Eitht Floor San Francisco, CA 94111-3834			ART UNIT	PAPER NUMBER
San Francisco,	CA 94111-3834		1642	
			DATE MAILED: 10/18/2004	.

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No.	Applicant(s) CARSON ET AL.	
Office Action Summary	09/847,102		
omee reason Gammary	Examiner	Art Unit	
The MAU INC DATE - (4.)	MISOOK YU, Ph.D.	1642	
The MAILING DATE of this communication apperiod for Reply	ppears on the cover sheet wi	ith the correspondence address	
A SHORTENED STATUTORY PERIOD FOR REPITHE MAILING DATE OF THIS COMMUNICATION - Extensions of time may be available under the provisions of 37 CFR 1 after SIX (6) MONTHS from the mailing date of this communication. - If the period for reply specified above is less than thirty (30) days, a repit find the period for reply is specified above, the maximum statutory period Failure to reply within the set or extended period for reply will, by status Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b). Status	136(a). In no event, however, may a reply within the statutory minimum of thirty did will apply and will expire SIX (6) MONT	eply be timely filed y (30) days will be considered timely.	
1) Responsive to communication(s) filed on <u>06 A</u>	<u> August 2004</u> .		
Za) ☐ This action is FINAL . 2b) ☑ This	s action is non-final		
3) Since this application is in condition for allowa	ance except for formal matte	ers. prosecution as to the merits is	
closed in accordance with the practice under I	Ex parte Quayle, 1935 C.D.	11, 453 O.G. 213.	
Disposition of Claims			
4) Claim(s) <u>1-8,16,28 and 29</u> is/are pending in the			
4a) Of the above claim(s) is/are withdraw	e application.		
5) Claim(s) is/are allowed.	wn from consideration.		
6) Claim(s) <u>1-8,16,28 and 29</u> is/are rejected.			
7) Claim(s) is/are objected to.			
8) Claim(s) are subject to restriction and/or	r election requirement		
	credion requirement.		
Application Papers			
9) The specification is objected to by the Examiner	r.		
10) The drawing(s) filed on is/are: a) acce	epted or b) objected to by	the Examiner	
represent may not request that any objection to the c	rawing(s) he held in abovenes	C 07 0ED 4	
replacement drawing sneet(s) including the correction	On is required if the drawing (-)	to the same of	
11) The oath or declaration is objected to by the Exa	aminer. Note the attached C	Office Action or form PTO-152	
riority under 35 U.S.C. § 119			
12) Acknowledgment is made of a claim for foreign p			
a) ☐ All b) ☐ Some * c) ☐ None of:	ononly under 35 U.S.C. § 11	19(a)-(d) or (f).	
1. Certified copies of the priority documents	hovo hoon was a		
2. Certified copies of the priority documents	have been received.		
Copies of the certified copies of the priorit application from the International Russesses	iv documents have been re-	ication No	
Femalian north the international burgall i	(PCT Rule 17.2/a))		
* See the attached detailed Office action for a list of	f the certified copies not rea	oive 4	
	and doranica copies hot reci	eiveg.	
achment(s)			
Notice of References Cited (PTO-892)			
Notice of Destination	4) Interview Summ	120/ (PTO 442)	
Notice of Draftsperson's Patent Drawing Review (PTO-948) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper Nots (Mail Date 08/05/04)	4) Interview Summ Paper No(s)/Ma	nary (PTO-413) nil Date nal Patent Application (PTO-152)	

2) 3)

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DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/03/2004 has been entered. Claims 1, 5, 16, and 28 are amended. Claims 1-8, 16, 28, and 29 are pending and examined on merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

This Office action contains new ground of rejection.

Claim Rejections - 35 USC § 112, Withdrawn

The rejection of claim 5 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 103, Withdrawn

The rejection of claims 1-8, 16, 22, 28, and 29 under 35 U.S.C. 103(a) as being unpatentable over any one of Tanaka et al (IDS, #1711998, Proc. Natl. Acad. Sci. USA. vol. 95, pages 10164-9), He et al (IDS # 93, 1997, Science vol. 275, pages 1652-4), or Wang et al (IDS #184, 1996, J. Biol. Chem. vol. 271, pages 4468-76) in view of Campbell, A. (1986, Monoclonal antibody technology, chapter 1 only, Elsevier Science Publishers B.V., Netherlands) is withdrawn in view of the amendment.

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The Following Are New Grounds of Rejection Claim Rejections - 35 USC § 112

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the malignant cell" in line 4. There is insufficient antecedent basis for this limitation in the claim. Amending the claim to "a malignant cell" in line 4, followed by "the malignant cell" in line 5 would obviate this rejection. This rejection affects all dependent claims.

Claims 1-8, 16, 28, and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

This new matter rejection is made because of the new limitation "the antibody inhibits growth of a malignant cell that expresses the frizzled 5 receptor" in the newly amended claims 1, and 16, the new limitation "wherein the antibody is effective for immunotherpay of a malignant cell that overexpresses the frizzled 5 receptor" in claim 28.

Applicant states that the support for the amendment is found at pages 21, 22, 25, and 26. However, the specification at page 21, and 25 discloses expression pattern of

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frizzled 2, and frizzled 5 detected by RT-PCR. The specification at page 22 discloses cell growth inhibition with an antibody binding to a frizzled receptor, but does not disclose "the antibody inhibits growth of a malignant cell that expresses the frizzled 5 receptor". The specification at page 26 discloses the effect of an anti-frizzled 2 antibody on growth of cancer cells, not the effect of an anti-frizzled 5 antibody on growth of a malignant cell that expresses the frizzled 5 receptor. This rejection affects all dependent claims.

Claims 1-8, 16, 28, and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are interpreted as drawn to an antibody binding to SEQ ID NO:68, or pharmaceutical comprising said antibody, wherein said antibody inhibits growth of a malignant cell that expresses the frizzled 5 receptor.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and

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8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The specification discloses that in comparison to normal epithelial cells, all HNSCC had markedly increased mRNA levels of frizzled-2. Treatment of one HNSCC cell line (SNU 1076) with an anti-frizzled 2 antibody inhibited proliferation and induced apoptosis in these cells (note Figs 4, 6, and Example 3).

The specification does not teach whether an anti-frizzled 5 antibody would inhibit growth of a malignant cell that expresses the frizzled 5 receptor. However, Rhee et al., (Sep. 26, 2002, Oncogene vol. 21, issue 43, pages 6598-605) teach at page 6599, left column, under the heading *Expression of Wnt and Fz mRNAs in HNSCC* that "When compared to the housekeeping gene G3PDH, all the Wnts, as well as Fz-2, were expressed more frequently in HNSCC than in normal cells, while there was no difference in Fz-5 gene expression". This suggests that the frizzled 5 receptor might not be expressed on a malignant cell. Note some of authors of the peer-reviewed journal article are the inventors of the instant application.

As for claims 16, and 29 reciting pharmaceutical and claim 28 reciting "effective for immunotherapy", Rhee et al., which was published two years after the instant application had been filed, discloses at page 6599, left column that "the Wnt and Fz genes are frequently overexpressed in HNSCC, and might be attractive targets for both immunotherapy and drug therapy." This suggests that some Wnt and Fz genes overexpressed in HNSCC might be attractive targets for both immunotherapy and drug therapy. This indicates that frizzled 5 receptor which is not overexpressed in those

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cancer cell lines tested does not appear to be a good target for immunotherapy or drug therapy. Further, even those frizzled genes that are overexpressed in the tested cancer cell lines, pharmaceutical development is a way in the future. In other words, a pharmaceutical against frizzled receptor overexpressed has not been developed yet. Inherent in pharmaceutical is in vivo use. The specification does not teach any antibody to instant SEQ ID NO:68 capable of treating any disease. Based on Rhee et al., one of skilled in the art has to screen a large clinical samples to see which malignant cell expresses the frizzled 5, followed by screening for an anti-frizzled 5 antibody capable of binding instant SEQ ID NO:68 that inhibits growth of a malignant cell or is effective. The specification has not even established whether frizzled 5 receptor overexpresses in any in vivo malignant cell as compared to normal healthy control, nor does the specification teach a single species of a purified antibody that binds to an extracellular domain of a frizzled 5 receptor, wherein the antibody inhibits growth of a malignant cell that expresses the frizzled 5 receptor.

It is noted that law requires that the disclosure of an application shall inform those skilled in the art how to make the alleged discovery, not how to screen it for them.

Considering the unpredictable state of art, limited guidance, no examples in the specification how to use the instantly claimed invention, broad breath of the claims, it is concluded that undue experimentation is required to practice the invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-

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272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey C Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.

Examiner
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